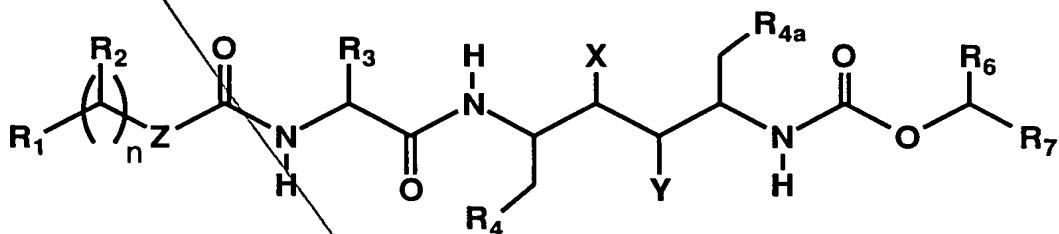


CLAIMS

What is claimed is:

see A1
1. A compound of the formula:



wherein R₁ is monosubstituted thiazolyl, monosubstituted oxazolyl, monosubstituted isoxazolyl or monosubstituted isothiazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy;

n is 1, 2 or 3;

R₂ is hydrogen or loweralkyl;

A'
Cont'd

R₃ is loweralkyl;

R₄ and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from

(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;

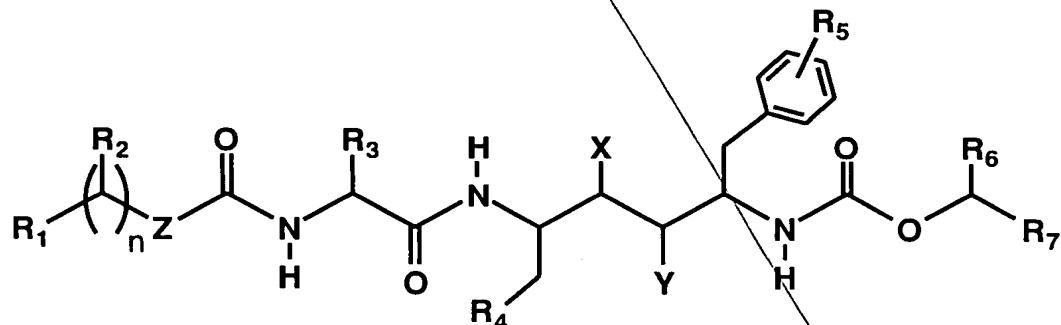
R₆ is hydrogen or loweralkyl;

R₇ is thiazolyl, oxazolyl, isoxazolyl or isothiazolyl wherein the thiazolyl, oxazolyl, isoxazolyl or isothiazolyl ring is unsubstituted or substituted with loweralkyl;

X is hydrogen and Y is -OH or X is -OH and Y is hydrogen, with the proviso that X is hydrogen and Y is -OH when Z is -N(R₈)- and R₇ is unsubstituted and with the proviso that X is hydrogen and Y is -OH when R₃ is methyl and R₇ is unsubstituted; and

Z is absent, -O-, -S-, -CH₂- or -N(R₈)- wherein R₈ is loweralkyl, cycloalkyl, -OH or -NHR_{8a} wherein R_{8a} is hydrogen, loweralkyl or an N-protecting group; or a pharmaceutically acceptable salt, ester or prodrug thereof.

2. A compound of the formula:



wherein R₁ is monosubstituted thiazolyl, monosubstituted oxazolyl, monosubstituted isoxazolyl or monosubstituted isothiazolyl wherein the

As Contd

substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy;

n is 1, 2 or 3;

R₂ is hydrogen or loweralkyl;

R₃ is loweralkyl;

R₄ is phenyl, thiazolyl or oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from (i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;

R₅ is hydrogen, halo, loweralkyl, hydroxy, alkoxy or thioalkoxy;

R₆ is hydrogen or loweralkyl;

R₇ is thiazolyl, oxazolyl, isoxazolyl or isothiazolyl wherein the thiazolyl, oxazolyl, isoxazolyl or isothiazolyl ring is unsubstituted or substituted with loweralkyl;

X is hydrogen and Y is -OH or X is -OH and Y is hydrogen, with the proviso that X is hydrogen and Y is -OH when Z is -N(R₈)- and R₇ is unsubstituted

and with the proviso that X is hydrogen and Y is -OH when R₃ is methyl and R₇ is unsubstituted;

A' cont'd

Z is absent, -O-, -S-, -CH₂- or -N(R₈)- wherein R₈ is loweralkyl, cycloalkyl, -OH or -NHR_{8a} wherein R_{8a} is hydrogen, loweralkyl or an N-protecting group; or a pharmaceutically acceptable salt, ester or prodrug thereof.

3. The compound of Claim 2 wherein R₁ is monosubstituted thiazolyl or monosubstituted oxazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi)cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy; n is 1; R₂ is hydrogen; R₄ is phenyl or thiazolyl; R₅ is hydrogen; R₆ is hydrogen and R₇ is thiazolyl, oxazolyl, isothiazolyl or isoxazolyl.

4. The compound of Claim 2 wherein R₁ is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi)cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent

A
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selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy; n is 1; R₂ is hydrogen; R₄ is phenyl; R₅ is hydrogen; R₆ is hydrogen and R₇ is 5-thiazolyl, 5-oxazolyl, 5-isothiazolyl or 5-isoxazolyl.

5. The compound of Claim 2 wherein R₁ is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is loweralkyl; n is 1; R₂ is hydrogen; R₄ is phenyl; R₅ is hydrogen; R₆ is hydrogen; R₇ is 5-thiazolyl, 5-oxazolyl, 5-isothiazolyl or 5-isoxazolyl; and Z is -O- or -N(R₈)- wherein R₈ is loweralkyl.

6. The compound of Claim 2 wherein R₁ is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is ethyl or isopropyl; n is 1; R₂ is hydrogen; R₃ is methyl or isopropyl; R₄ is phenyl; R₅ is hydrogen; R₆ is hydrogen; R₇ is 5-thiazolyl, 5-oxazolyl, 5-isothiazolyl or 5-isoxazolyl; and Z is -O-.

7. The compound of Claim 2 wherein R₁ is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is ethyl or isopropyl; n is 1; R₂ is hydrogen; R₃ is isopropyl; R₄ is phenyl; R₅ is hydrogen; R₆ is hydrogen; R₇ is 5-thiazolyl, 5-oxazolyl, 5-isothiazolyl or 5-isoxazolyl; Z is -N(R₈)- wherein R₈ is methyl; X is hydrogen and Y is -OH.

B
cont'd

8. (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; or a pharmaceutically acceptable salt, ester or prodrug thereof.

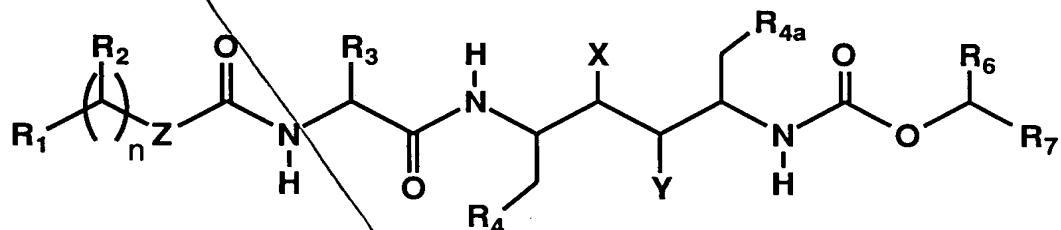
Part 4
~~9 (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-oxazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

see A2
~~10. A compound selected from the group consisting of:
(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)alaninyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-2-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)valinyl)amino)-5-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)alaninyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-((2-(N,N-Dimethylamino)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-2-(N-(N-((2-(N,N-Dimethylamino)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-5-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-((2-(4-Morpholinyl)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-2-(N-(N-((2-(4-Morpholinyl)-4-thiazolyl)methoxycarbonyl)valinyl)-amino)-5-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-((2-(1-Pyrrolidinyl)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;~~

A2
cont'd)

(2S,3S,5S)-5-(N-(N-Methyl-N-((2-isopropyl-4-oxazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-oxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-oxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;
(2S,3S,5S)-5-(N-(N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-isoxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; and
(2S,3S,5S)-5-(N-(N-Methyl-N-((2-isopropyl-4-oxazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-isoxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; or a pharmaceutically acceptable salt, ester or prodrug thereof.

11. A compound of the formula:



wherein R₁ is monosubstituted thiazolyl, monosubstituted oxazolyl, monosubstituted isoxazolyl or monosubstituted isothiazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected

from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy;

~~n is 1, 2 or 3;~~

~~R₂ is hydrogen or loweralkyl;~~

~~R₃ is loweralkyl;~~

~~R₄ and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from~~

~~(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;~~

~~R₆ is hydrogen or loweralkyl;~~

~~R₇ is thiazolyl, oxazolyl, isoxazolyl or isothiazolyl wherein the thiazolyl, oxazolyl, isoxazolyl or isothiazolyl ring is unsubstituted or substituted with loweralkyl;~~

~~X is -OH and Y is -OH; and~~

~~Z is absent, -O-, -S-, -CH₂- or -N(R₈)- wherein R₈ is loweralkyl, cycloalkyl, -OH or -NHR_{8a} wherein R_{8a} is hydrogen, loweralkyl or an N-protecting group; or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

*sub
B 2*

~~12. A method for inhibiting HIV protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 1.~~

~~13. A method for inhibiting HIV protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 2.~~

sub B3
14. A method for inhibiting ~~HIV~~ protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 8.

15. A method for inhibiting ~~HIV~~ comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 1.

16. A method for inhibiting HIV comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 2.

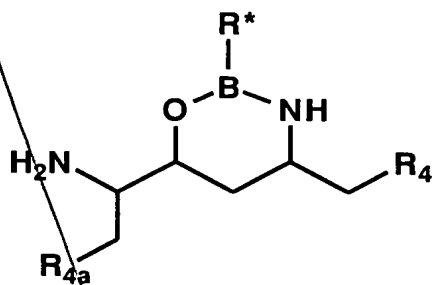
17. A method for inhibiting HIV comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 8.

18. ¹⁴ A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 1.

19. ¹⁵ A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 2.

20. A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 8.

21. A compound of the formula:

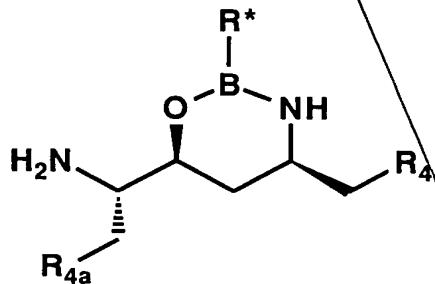


wherein R_4 and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from

(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy; and R^* is phenyl, halo-substituted phenyl, dihalo-substituted phenyl, alkoxy-substituted phenyl, loweralkyl-substituted phenyl, bis-trifluormethyl-substituted phenyl or naphthyl or loweralkyl; or an acid addition salt thereof.

22. The compound of Claim 21 wherein R_4 and R_{4a} are phenyl and R^* is phenyl.

23. A compound of the formula:



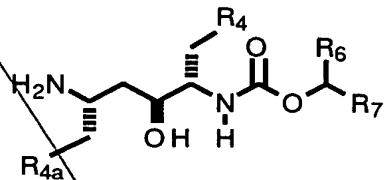
wherein R_4 and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from

(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy; and

R^* is phenyl, halo-substituted phenyl, dihalo-substituted phenyl, alkoxy-substituted phenyl, loweralkyl-substituted phenyl, bis-trifluormethyl-substituted phenyl or naphthyl or loweralkyl; or an acid addition salt thereof.

24. The compound of Claim 23 wherein R_4 and R_{4a} are phenyl and R^* is phenyl.

25. A process for the preparation of a compound of the formula:

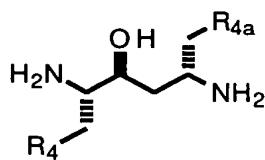


wherein R_4 and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from

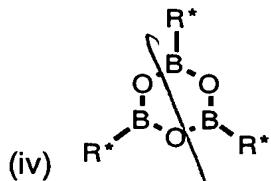
(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;

R_6 is hydrogen or loweralkyl; and

R_7 is thiazolyl, oxazolyl, isoxazolyl or isothiazolyl wherein the thiazolyl, oxazolyl, isoxazolyl or isothiazolyl ring is unsubstituted or substituted with loweralkyl; or an acid addition salt thereof, comprising (a) reacting a compound of the formula:



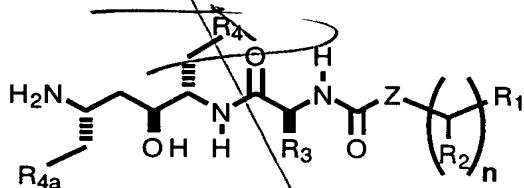
wherein R_4 and R_{4a} are defined as above with (i) $R^*B(OH)_2$, (ii) $B(OR^{**})_3$, (iii) $B(R^{***})_3$ or



wherein R* is phenyl, halo-substituted phenyl, dihalo-substituted phenyl, alkoxy-substituted phenyl, loweralkyl-substituted phenyl, bis-trifluormethyl-substituted phenyl or naphthyl or loweralkyl, R** is loweralkyl and R*** is halo, followed by (b) acylating the product of step (a) with a compound of the formula (R₆)(R₇)CHOC(O)OL wherein L is an activating group for the acylation reaction and wherein R₆ is and R₇ are defined as above

26. The process of Claim 25 wherein R₄ and R_{4a} are phenyl and R* is phenyl or R** is isopropyl.

27. A process for the preparation of a compound of the formula:



wherein R₁ is monosubstituted thiazolyl, monosubstituted oxazolyl, monosubstituted isoxazolyl or monosubstituted isothiazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, (vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii)

\(heterocyclic)alkyl wherein heterocyclic is defined as above, (ix) alkoxyalkyl, (x) thioalkoxyalkyl, (xi) alkylamino, (xii) dialkylamino, (xiii) phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (xiv) phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, (xv) dialkylaminoalkyl, (xvi) alkoxy and (xvii) thioalkoxy;

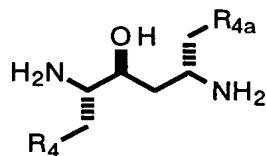
n is 1, 2 or 3;

R₂ is hydrogen or loweralkyl;

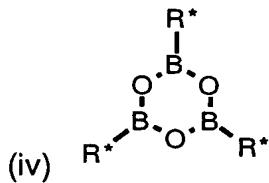
R₃ is loweralkyl; and

R₄ and R_{4a} are independently selected from phenyl, thiazolyl and oxazolyl wherein the phenyl, thiazolyl or oxazolyl ring is unsubstituted or substituted with a substituent selected from

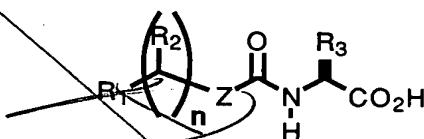
(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy; or an acid addition salt thereof, comprising (a) reacting a compound of the formula:



wherein R₄ and R_{4a} are defined as above with (i) R^{*}B(OH)₂, (ii) B(OR^{**})₃, (iii) B(R^{***})₃ or



wherein R^* is phenyl, halo-substituted phenyl, dihalo-substituted phenyl, alkoxy-substituted phenyl, loweralkyl-substituted phenyl, bis-trifluormethyl-substituted phenyl or naphthyl or loweralkyl, R^{**} is loweralkyl and R^{***} is halo, followed by (b) reacting the product of step (a) with a compound of the formula:



or an activated ester derivative thereof, wherein R_1 , R_2 , R_3 , Z and n are defined as above.

28. The process of Claim 27 wherein R_4 and R_{4a} are phenyl and R^* is phenyl or R^{**} is isopropyl.

*add
A3*

*add
B5*

*add
E2*